Remarks

Section 112, 2nd Paragraph

Claim 18 was found indefinite. Specifically, claim 18 is found to recite the limitation "fixed erythrocyte". The Office action noted that it "is unclear in what way said erythrocyte is "fixed" and what exactly it is fixed to, as the instant claims do not recite any methods steps directed to fixing erythrocytes."

A fixed cell (such as an erythrocyte) is a very well known term. McGraw-Hill Dictionary of Scientific and Technical Terms, Sixth Edition defines "fix" as: "To kill, harden or preserve a tissue, organ, or organism by immersion in dilute acids, alcohol, or solutions of coagulants." In Molecular Biology of the Cell, 2nd Edition, notes "fixation makes cells permeable to staining reagents and cross-links their macromolecules so that they are stabilized and locked in position. Some of the earliest procedures involved immersion in acids or in organic solvents such as alcohol. Current procedures usually include treatment with reactive aldehydes, particularly formaldehyde and glutaraldehyde, which form covalent bonds with the free amino groups of proteins and thereby cross link adjacent molecules."

These definitions of the term "fixed" are consistent with how the applicant has used the term in the specification. For example, on page 6, the applicants note, "it is possible to work with fixed erythrocytes (conserved using formaldehyde or glutaraldehyde) as well as unfixed (native) ones. From a practical point of view it is advised to work with fixed erythrocytes (one single fixation step sufficient for a couple of experiments)."

The term "fixed cells", of which "fixed erythrocytes" is but one example, is very well understood to those of ordinary skill in the art. Those understanding this term would know both what it means and would know how to create fixed cells. From the usage within the specification, it would be known the way in which such cells could be fixed and the methods of fixation of said cells. Given these facts, the present claim is definite and the instant rejection should be reconsidered and withdrawn.

Section 103

The sole remaining issue is whether the applicant's claims are rendered obvious by a combination of references. Again, reconsideration is warranted.

In making an obviousness rejection, the Examiner must first determine the scope and content of the prior art, ascertain the differences between the prior art and the claims in issue, and resolve the level of ordinary skill in the art. Graham v. John Deere 148 USPQ 459 (1966). In order to establish a *prima facie* case of obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 180 USPQ 580 (CCPA 1974). Under these standards the present claims are not obvious.

Claims 16-19, 21, 24-26, and 28 were found obvious under Henon et al. in view of Jan et al. Henon et al. is cited for a number of elements claimed in independent claim 1, but the Office action acknowledges, "Henon et al. do not specifically teach adhering erythrocytes to "target cells"". Instead this reference merely notes that the geometry of red blood cells can be altered. The Office action then fails to cite anything from the second reference to teach this missing claim element. Nothing in Jan et al. teaches adhering to at least one target cell at least one auxiliary object, wherein

an erythrocyte is one of the auxiliary objects. Instead, the second reference is cited as "Jan et al. teach methods for analyzing the role of surface electric charge in red blood cell interactions wherein erythrocytes (e.g. auxiliary cells) are coated with substances that change the surface charge of the erythrocyte". This teaching actually teaches away from the present claims. Given that at least one of the claimed steps in the method of claim 16 is not found in the cited references, this claim is not rendered obvious by the cited reference. The Applicant also notes that the alternative auxillary objects, including haemoglobin, haemoglobin derivatives, chromophore or chloroplasts are also not disclosed in the cited reference.

For at least the same reason as claim 16 is allowable, claims 18 and 19, which depend on claim 18 and 19 which depend on claim 16 should also be allowed.

With respect to claim 21, the Office action again fails to disclose, in either of the references, a target cell and an adherent auxiliary object, such as an erythrocyte. This system requires an adherent auxiliary object, such as an erythrocyte, that is aligned with the laser beam. Not only is this not disclosed in the cited reference, Henon et al. actually teaches away from the claimed system by aligning the beam not with the red blood cells but instead with the beads.

In the present patent claims, the applicant has recognized that red blood cells and other auxiliary objects are superior to beads as force transducers for axial deformation (i.e. a force with direction into the cell or way from it surface.) The auxiliary objects have a chromophore allowing the object to be used as a force transducer and force amplifier. This can be contrasted with Henon et al., a reference that teaches the to apply force to cells via beads. As is repeatedly stressed in Henon et al., force is applied to the beads, not the red blood cells, for moving the cells.

This is the exact opposite of what is claimed, using cells as the auxiliary object onto which the force is directed.

Claims 24-26, and 28 each depend from claim 21 and should be found allowable for at least the same reasons claim 21 is allowable.

In addition to failing to teach the claimed elements, there is no proper cited teaching to combine the two cited references. The motivation to combine the references as cited in the Office action is: "it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to adhere chemically aggregated erythrocytes taught by Jan et al. with bead bound erythrocytes using the optical using the optical tweezer method and system of Hennon et al., where the motivation would have been a clinical interest in developing improved methods for inhibiting blood cell aggregation [Jan et al. abstract]." However, Jan et al. actually state that their "present experiments were designed to study the role or RBC surface charge in affecting the effectiveness of dextrans . . . in inducing RBC aggregation." Jen et al., p. 638. Rather than inhibiting aggregation, as the Office action suggests, Jan et al. actually examine the induction of RBC aggregation. This stands in contrast to the incompatible teachings of Hennon, which is a study of erythrocyte membrane elasticity. Such a study requires free erythrocytes in suspension rather than adherent cells. The very notion that an experimenter would adhere aggregated erythrocytes by a motivation to inhibit blood cell aggregation does not make logical sense. This appears to state that one would clump cells together motivated by a desire not to clump cells together. The presented reason indicates that the two cited references teach at cross-purposes and would not be combined to reach the applicants claims. This provides a second, independent reason to reconsider the present rejections.

Next, claims 16-19, 21, 24-26, 28, and 29 were found rendered obvious by Visscher et al. in view of Jan et al. and Shaw et al. Again, the Applicants respectfully traverse the present rejection.

Visscher et al. have developed a micromanipulator employing multiple optical traps created by a single beam. This is demonstrated using bacterial cells that are directly trapped. On page 113, the authors also note that indirect trapping is possible using beads. In one such example, the beads are coated with monoclonal antibodies. Visscher et al. does not teach adhering a target cell to an erythrocyte. Jan et al. also does not teach adhering a target cell to an erythrocyte to a target cell, but instead merely explores conditions under which red blood cells aggregate together. Shaw et al. also do not teach this lacking claim element. Given that at least one element of claim 16, namely adhering a target cell and an auxiliary object such as an erythrocyte, is not found in the cited reference this combination of references does not render the applicant's claim 16 obvious.

Claims 17-19 depend on claim 16. For at least the same reason as claim 16 is not rendered obvious, claims 17-19 are also not rendered obvious by the cited reference.

Claim 21 is directed to a system including a target cell and an adherent auxiliary object such as an erythrocyte. As already noted, none of the cited references teach this element. Instead, Visscher et al. teach away from this element by disclosing that it already has a preferred method of moving target cells, namely using beads as an auxiliary object.

Claims 24-26, and 28 depend on claim 21. For at least the same reason claim 21 is allowable, claims 24-26, and 28 should also be allowed.

In addition to failing to teach all of the claimed elements, the present Office action also does not cite a proper teaching to combine the references. Visscher et al. already have an object to allow the application of pressure to a cell, namely a bead. Given that a working solution already exists to the need to apply forces to bacterial cells using auxiliary objects. The cited references actually teach away from the cited combination. This provides a second, independent reason to reconsider the instant rejection.

Conclusion

Applicant respectfully requests reconsideration in light of the submitted remarks. A Notice of Allowance is earnestly solicited. If any matter relating to this case needs to be discussed please call our office at (408) 297-9733 between 9 a.m. and 5 p.m. Pacific time.

CERTIFICATE OF MAILING

I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being transmitted via the Office electronic filing system in accordance with § 1.6(a)(4) on the date shown below.

Signed: Sally Azevedo
Typed Name: Sally Azevedo

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